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- (71) Applicant (*for all designated States except US*): THE QUEEN'S UNIVERSITY OF BELFAST [GB/GB]; University Road, Belfast BT7 1NN (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): SEDDON, Kenneth, Richard [GB/GB]; Tara, 145 Millisle Road, Donaghadee BT21 0LA (GB). CARMICHAEL, Adrian, John [GB/GB]; University of Warwick, Lakeside Apartments, Staff Flat 3, Coventry CV4 7AL (GB). EARLE, Martyn, John [GB/GB]; 40A Inishowen Drive, Finaghy, Belfast BT10 0EU (GB).
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(54) Title: PROCESS FOR PREPARING AMBIENT TEMPERATURE IONIC LIQUIDS

(57) Abstract: A process for preparing an ionic liquid or salt, preferably in which the cation comprises an N-alkylated base and the anion is a carboxylate, formed by reaction between an organic base and an alkylating agent, wherein the alkylating agent is a fluorinated ester or an alkyl sulfonate, is described. Suitable organic bases include imizadoles, substituted imidazoles, pyridines and substituted pyridines. The so-formed products can be subsequently transformed into different ionic liquids or salts by metathesis.

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10 "Process for Preparing Ambient Temperature Ionic  
11 Liquids"

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13 This invention relates to a process for processing  
14 ambient temperature ionic liquids.

15

16 Ambient temperature ionic liquids based upon the 1,3-  
17 dialkylimidazolium cation were first reported in 1982  
18 by Wilkes et al<sup>1</sup>. These systems were based upon the  
19 chloroaluminate anion and although they possess many  
20 useful properties (e.g. wide liquids, thermal stability  
21 and large electrochemical window) they are reactive to  
22 certain materials and are sensitive to moisture. An  
23 air and water stable system was developed by Wilkes and  
24 Zaworotko in 1992 based upon the tetrafluoroborate  
25 anion<sup>2</sup>. Since this report a wide range of ionic liquids  
26 containing different anions have appeared in the  
27 literature<sup>3</sup>. These systems have received much attention  
28 and recent studies have shown that ambient temperature  
29 ionic liquids can be used as solvents for a range of  
30 chemical reactions including polymerisation<sup>4</sup>.

1 hydrogenation<sup>5</sup>, Friedel-Crafts acylations<sup>6</sup> and for the  
2 Diels-Alder reaction<sup>7</sup>.

3

4 The principal route currently employed in the synthesis  
5 of the air and moisture stable 1,3-dialkylimidazolium  
6 ionic liquids is outlined in Scheme 1.

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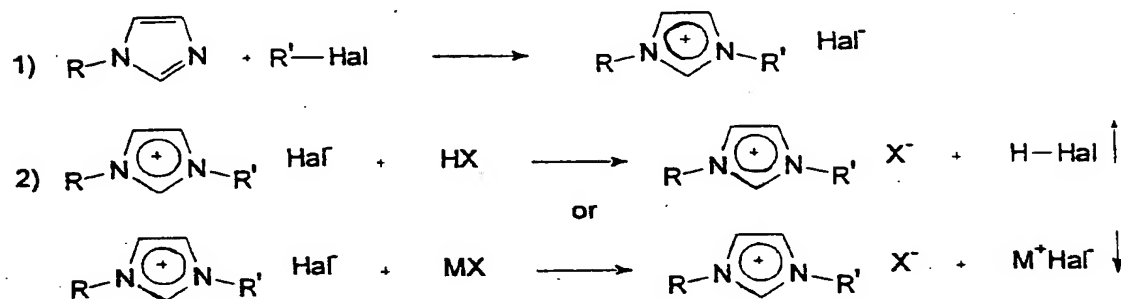
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Scheme 1.

The first step with this method is the alkylation of 1-alkylimidazole with a haloalkane to give a 1,3-dialkylimidazolium halide salt. The second step is metathesis of the halide for the appropriate anion. The second step can be carried out with either an acid or a metal salt to eliminate H-Hal as or precipitate M<sup>+</sup>Hal<sup>-</sup> respectively. It is here that the intrinsically good solvating properties of these ionic liquids become a problem. In many of the syntheses the ionic liquids

1 solvate the halide waste so effectively that complete  
2 removal is not effected. Halide contamination of the  
3 ionic liquids is a problem that must be overcome for  
4 them to be used as reaction solvents on a large scale.  
5 For instance, when used as media for transition metal  
6 catalysed reactions the presence of strongly co-  
7 ordinating halide ions have been shown to reduce  
8 catalyst activity<sup>5</sup>. The opportunity exists in many  
9 reactions for the residual halides to be oxidised to  
10 halogens which will result with many substrates and can  
11 corrode apparatus. In addition, this method always  
12 generates a stoichiometric amount of halide salt as a  
13 waste product. When metathesis is carried out using a  
14 silver salt the route becomes prohibitively expensive  
15 upon scale up. Employing the alkali metal salts  
16 reduces the cost, but not the waste.

17

18 We have developed a new method for the synthesis of the  
19 air- and moisture-stable ionic liquids that overcomes  
20 the possibility of halide impurities and reduces the  
21 amount of waste products. This method is based upon  
22 the use of fluorinated esters or alkyl sulfonates as  
23 replacements for haloalkanes.

24

25 Thus, according to one aspect of the present invention,  
26 there is provided a process for preparing an ionic  
27 liquid or salt formed by reaction between an organic  
28 base and an alkylating agent, wherein the alkylating  
29 agent is a fluorinated ester or an alkyl sulfonate.

30

31 The so-formed product of the organic base and ester or  
32 sulfonate could subsequently be transformed into a

1 different ionic liquid or salt with a range of  
2 different anions by metathesis, preferably using an  
3 acid or metal salt.

4

5 In one embodiment of the present invention, the cation  
6 formed is an N-alkylated base.

7

8 For this, the organic base could be an imidazole or a  
9 substituted imidazole. Preferably, the substituted  
10 imidazolium salt is a 1,3-dialkylimidazolium  
11 trifluoroethanoate and the (n-1)-substituted imidazole  
12 is a 1-alkylimidazole.

13

14 Alternatively, the organic base is a pyridine or a  
15 substituted pyridine.

16

17 Other organic bases include the phosphines and  
18 sulfides.

19

20 Also preferably a co-solvent is used.

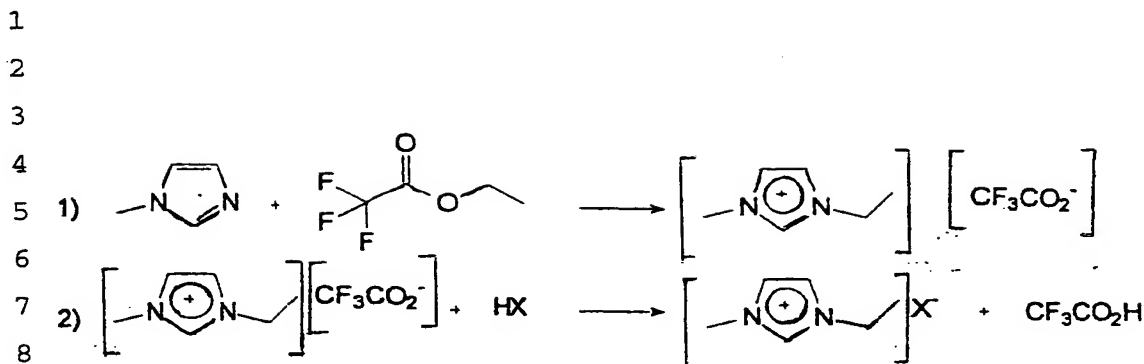
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22 The following description will focus on using the  
23 organic base 1-methylimidazole, the imidazole most  
24 commonly used in the preparation of ambient temperature  
25 ionic liquids, and ethyl trifluoroethanoate as the  
26 alkylating agent.

27

28 The synthesis is similar to that mentioned above in  
29 Scheme 1, in that there is an alkylation and a  
30 metathesis step to give the desired ionic liquid as  
31 shown in Scheme 2.

32



10

11 Scheme 2.

12

13 The reaction of 1-methylimidazole with ethyl  
14 trifluoroethanoate to give 1-ethyl-3-methylimidazolium  
15 trifluoroethanoate, [emim][TFA], proceeds cleanly and  
16 smoothly at moderate temperature (70°C). However, some  
17 reduction in the rate of reaction may occur as the  
18 reaction proceeds. The primary reason for the  
19 reduction in rate is that unreacted 1-methylimidazole  
20 concentrates in the ionic liquid phase as it forms,  
21 while the ethyl trifluoroethanoate is only slightly  
22 soluble in [emim][TFA]; thus reactants are kept apart.  
23 Addition of a co-solvent to solubilise reactants and  
24 products, for example acetonitrile, overcomes this  
25 problem and a significant rate enhancement is observed.  
26 Alternatively, the reaction may be performed in an  
27 autoclave.

28

29 [emim][TFA] is an ambient temperature ionic liquid with  
30 all the expected characteristics in its own right. In  
31 addition, it is a good starting point for the synthesis

1 of other air- and moisture-stable ionic liquids with  
2 metathesis of the trifluoroethanoate anion easily  
3 achieved. Addition of the desired acid to [emim][TFA]  
4 yields a reaction mixture with only one volatile  
5 material, trifluoroethanoic acid (b.pt.72 °C), which is  
6 easily removed under vacuum. This is true as long as  
7 the added acid is of higher boiling point than  $\text{CF}_3\text{CO}_2\text{H}$ ,  
8 which most acids of interest are (e.g.  $\text{HPF}_6$ ,  $\text{HBF}_4$ ,  
9  $\text{H}_3\text{PM}_{12}\text{O}_{40}$  (M = W, Mo),  $\text{H}_3\text{PO}_4$ ). This gives the desired  
10 ionic liquid, without extractions and washings, in a  
11 halide free state.

12

13 The use of longer alkyl chain esters (e.g. hexyl  
14 trifluoroethanoate) works equally as well with 1-  
15 alkylimidazoles to give the desired product. The use  
16 of more fluorinated esters (e.g. ethyl  
17 heptafluorobutanoate) is still possible although they  
18 may have the drawback of generating a less volatile  
19 carboxylic acid by-product.

20

21 Alkyl sulfonates for use as the alkylating agent are  
22 also well known in the art, such as a methyl sulfonate;  
23 more particularly butyl methylsulfonate.

24

25 According to a second aspect of the present invention  
26 there is provided a process for preparing an ionic  
27 liquid or salt formed by reaction between an organic  
28 base and fluorinated alkylating agent whenever the so-  
29 formed fluorinated by-product has a lower boiling point  
30 than the acid added to the alkylating agent.

31

1 The cation formed is preferably an N-alkylated base.  
2 This is a general method that can be used to synthesise  
3 a range of (imidazolium, possibly substituted  
4 imidazolium) ionic liquids and low melting point salts.

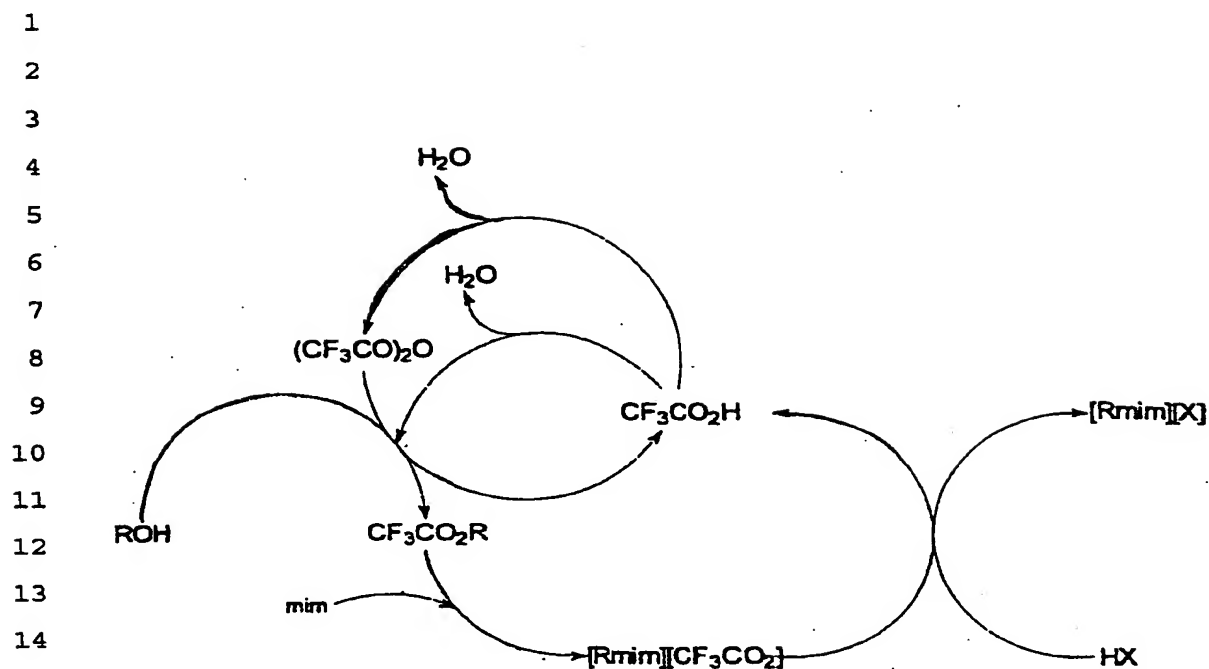
5  
6 The present invention extends to any product obtainable  
7 from any of the new processes herein described.  
8 Particularly, it extends to a 1,3-dialkylimidazolium-  
9 based ionic liquid whenever prepared by reacting  
10 1-alkylimidazole with a fluorinated ester, followed by  
11 metathesis.

12  
13 The present invention also extends to the use of any  
14 ester able to act in a similar manner to form an  
15 ambient temperature ionic liquid with an organic base.

16  
17 The reaction conditions required to effect the  
18 processes of the present invention will be known or  
19 calculable to those skilled in the art.

20  
21 The use of fluorinated compounds, although expensive,  
22 is desired for two reasons. Firstly, fluorination of  
23 the ester activates the molecule for the alkylation  
24 step, and secondly, fluorinated products are more  
25 volatile and of lower boiling point than their non-  
26 fluorinated analogues, thus making separation of the  
27 ionic liquid easier. The cost of using fluorinated  
28 esters should not be prohibitively expensive as the  
29 carboxylic acid by-product can be recycled. An overall  
30 process is envisaged as shown in Scheme 3.





Scheme 3

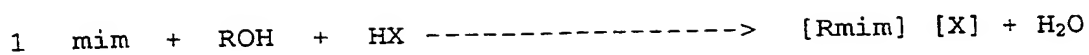
R = hydrocarbyl, or substituted hydrocarbyl.

X = any anion such as nitrate, tetrafluoroborate, hexafluorophosphate, etc.

mim = 1-methylimidazole.

R and X are used in their normal context as is well known in the art.

As scheme 3 shows, the waste trifluoroethanoic acid is recovered and converted into the reactive ester either through a straight esterification or via the anhydride. This gives the following balanced equation for the synthesis of ambient temperature ionic liquids;



2

3    The present invention thus provides a new synthetic  
4    route to ambient temperature ionic liquids that ensures  
5    the product is halide-free. If the metathesis is  
6    performed with an acid rather than a metal salt, then  
7    the product will be both halide-free and metal-free.  
8    In addition, the alkylating agent can be regenerated  
9    from inexpensive and readily available materials, thus  
10    reducing waste.

11

## 12    **Experimental**

13

### 14    **Preparation of 1-ethyl-3-methylimidazolium** 15    **trifluoroethanoate, [emim][TFA].**

16

17    1-Methylimidazole (2.5g, 30.4mmol) and ethyl  
18    trifluoroethanoate (25.8g, 181.6mmol) were dissolved in  
19    ethanenitrile (20cm<sup>3</sup>). The resultant solution was  
20    placed in a sealed glass vessel and stirred at 70°C for  
21    5 days giving a pale yellow solution. The volatiles  
22    were removed in vacuo giving [emim][TFA] in 100% yield.

23

### 24    **Preparation of 1-ethyl-3-methylimidazolium** 25    **tetrafluoroborate, [emim][BF<sub>4</sub>]**

26

27    To [emim][TFA] (1.0g, 4.5mmol) was added one equivalent  
28    of fluoroboric acid (0.412cm<sup>3</sup> of 10.8M aq. solution, 4.5  
29    mmol) and the mixture was stirred overnight at room  
30    temperature. Heating under vacuum at 100°C removes  
31    trifluoroethanoic acid and water giving [emim][BF<sub>4</sub>].

1 **Preparation of 1-ethyl-3-methylimidazolium**  
2 **hexafluorophosphate, [emim][PF<sub>6</sub>]**

3  
4 To [emim][TFA] (2.0g, 8.9mmol) dissolved in water  
5 (10cm<sup>3</sup>) was added hexafluorophosphoric acid (2cm<sup>3</sup> of  
6 6.79M aq. solution, 13.58mmol). This gave [emim][PF<sub>6</sub>]  
7 as a white precipitate which was collected by vacuum  
8 filtration.

9  
10 **Preparation of butyl methanesulfonate (BuOMs)**

11  
12 To a 500 cm<sup>3</sup> round-bottomed flask, equipped with a  
13 magnetic stirrer and pressure equalising dropping  
14 funnel, was added butanol (55.6 g, 0.75 mol),  
15 triethylamine (55.7 g, 0.55 mol) and dichloromethane  
16 (300 cm<sup>3</sup>). Methanesulfonyl chloride (57.3 g, 0.05 mol)  
17 was then added dropwise over a two-hour period from the  
18 dropping funnel, with cooling from an ice bath. The  
19 mixture was stirred for a further 24 hours at room  
20 temperature. The reaction mixture was filtered,  
21 concentrated on a rotary evaporator, and distilled (bp  
22 - 80-90 °C at 5 mm Hg). This gave 68.1 g (98%) of a  
23 colourless oil.

24  
25 **Preparation of 1-butyl-3-methylimidazolium**  
26 **methanesulfonate ([bmim][Oms])**

27  
28 In a 100 cm<sup>3</sup> round-bottomed flask, was added butyl  
29 methanesulfonate (15.3 g, 0.10 mol) and  
30 1-methylimidazole (8.21g, 0.10mol). A reflux condenser  
31 was attached and the mixture heated at 100 °C for 48

1 hours. A vacuum was applied to the flask (1 mm Hg) to  
2 remove unreacted starting materials for 12 hours at  
3 80 °C. The low-melting salt [bmim][Oms] (22.3 g, 95%)  
4 solidified on cooling.

5

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1     CLAIMS

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- 3     1.    A process for preparing an ionic liquid or salt  
4           formed by reaction between an organic base and an  
5           alkylating agent, wherein the alkylating agent is a  
6           fluorinated ester or an alkyl sulfonate.
- 7
- 8     2.    A process as claimed in Claim 1 wherein the cation  
9           formed is an N-alkylated base.
- 10
- 11    3.    A process as claimed in Claim 2 wherein the organic  
12          base is an imidazole or a substituted imidazole.
- 13
- 14    4.    A process as claimed in Claim 3 wherein the organic  
15          base is a 1-alkylimidazole.
- 16
- 17    5.    A process as claimed in Claim 4 wherein the organic  
18          base is 1-methylimidazole.
- 19
- 20    6.    A process as claimed in Claim 2 wherein the organic  
21          base is a pyridine or a substituted pyridine.
- 22
- 23    7.    A process as claimed in Claim 6 wherein the organic  
24          base is an alkylpyridine.
- 25
- 26    8.    A process as claimed in Claim 1 wherein the organic  
27          base is a phosphine or a sulphide
- 28
- 29    9.    A process as claimed in any one of the preceding  
30          Claims wherein a co-solvent is used.
- 31
- 32    10.   A process as claimed in Claim 9 wherein the co-  
33          solvent is acetonitrile.

- 1
- 2 11. A process as claimed in any one of the preceding
- 3 Claims wherein the reaction is carried out under
- 4 pressure.
- 5
- 6 12. A process as claimed in any one of the preceding
- 7 Claims wherein the anion formed is
- 8 trifluoroethanoate.
- 9
- 10 13. A process as claimed in any one of the preceding
- 11 Claims wherein the alkylating agent is ethyl
- 12 trifluoroethanoate.
- 13
- 14 14. A process as claimed in any one of Claims 1-12
- 15 wherein the alkylating agent is a methyl sulfonate.
- 16
- 17 15. A process as claimed in Claim 14 wherein the
- 18 alkylating agent is butyl methylsulfonate.
- 19
- 20 16. A process as claimed in any one of the preceding
- 21 Claims wherein the so-formed product is subsequently
- 22 transformed into a different ionic liquid or salt by
- 23 metathesis.
- 24
- 25 17. A process as claimed in Claim 16 wherein an acid or
- 26 metal salt is used for the metathesis.
- 27
- 28 18. A process for preparing an ionic liquid or salt
- 29 formed by reaction between an organic base and
- 30 fluorinated alkylating agent whenever the so-formed
- 31 fluorinated by-product has a lower boiling point
- 32 than the acid added to the alkylating agent.
- 33

- 1     19. An ionic liquid or salt whenever prepared by a  
2       process as claimed in Claims 1-18.  
3
- 4     20. A 1, 3-dialkylimidazolium trifluoroethanoate  
5       whenever prepared by a process as claimed in any one  
6       of Claims 1-18.  
7  
8



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/04584

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07B37/02 B01J31/02 B01J37/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07B B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 21871 A (BP CHEM INT LTD ; ABDUL SADA ALA A K (GB); AMBLER PHILIP WILLIAM (G) 17 August 1995 (1995-08-17) cited in the application the whole document	1
X	BEILSTEIN INFORMATION SERVICE; FILE: XFIRE , XP002163372 see BRN: 7736754 & HOWARTH ET AL.: TETRAHEDRON LETT., vol. 38, no. 17, 1997, pages 3097-3100,	20

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☒ Patent family members are listed in annex.

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European Patent Office, P.B. 5818 Patentlaan 2  
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